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			TCCG		C GA	GTAG	GGCC	AGG	TGTT	GGG	AGCT	CCCA	CG T	GGGA	CAAGG	6 <b>0</b> 77
atg Met 1	g <b>gt</b> Gly	ttc Phe	aac Asn	ctg Leu 5	cag Gln	gct Ala	ctc Leu	ctg Leu	gag Glu 10	cag Gln	ctc Leu	ag <b>c</b> Ser	cag Gln	gat Asp 15	g <b>ag</b> Glu	125
itg Leu	agc Ser	aag Lys	ttc Phe 20	aag Lys	tat Tyr	ctg Leu	atc	acg Thr 25	acc Thr	ttc Phe	tcc Ser	ccg Pro	gca Ala 30	ca <b>c</b> His	g <b>ag</b> Glu	173
ctc Leu	cag Gln	aag Lys 35	atc Ile	ccc Pro	cac	aag Lys	gag Glu 40	gta Val	gac Asp	aag Lys	gct Ala	gat Asp 45	ggg Gly	aag Lys	caa Gln	221
ctg Leu	gta Val 50	gaa Glu	atc Ile	ctc Leu	acc Thr	acc Thr 55	cat His	tgt Cys	gac Asp	agc Ser	tac Tyr 60	tgg Trp	gtg Val	gag Glu	atg Met	269
gcg Ala 65	agc Ser	ctc Leu	cag Gln	gtc Val	ttt Phe 70	gaa Glu	aag Lys	atg Met	cac His	cga Arg 75	atg Met	gat Asp	ctg Leu	tct Ser	gag Glu 80	317
aga Arg	gca Ala	aag Lys	gat Asp	gaā Glu 85	gtc Val	aga Arg	gaa Glu	gca Ala	gct Ala 90	ttg Leu	aaa Lys	tcc Ser	ttt Phe	aat Asn 95	a <b>aa</b> Lys	365
agg Arg	aag Lys	cct Pro	cta Leu 100	tca Ser	tta Leu	ggg Gly	ata Ile	aca Thr 105	cgg Arg	aaa Lys	gaa Glu	cga Arg	cca Pro 110	cct Pro	cta Leu	413
gac Asp	gtg Val	gac Asp 115	gaa Glu	atg Met	ctg Leu	gag Glu	cgc Arg 120	ttc Phe	aaa Lys	aca Thr	gaa Glu	gca Ala 125	caa Gln	gac Asp	a <b>aa</b> Lys	461
gac Asp	aat Asn 130	agg Arg	tgc Cys	agg Arg	tat Tyr	ata Ile 135	ttg Leu	aag Lys	acg Thr	aag Lys	ttc Phe 140	cgg Arg	gag Glu	atg M <b>et</b>	tgg	509
aag Lys 145		tgg Trp	cct Pro	gga Gly	gat Asp 150	agc Ser	aaa Lys	gag Glu	gtc Val	cag Gln 155	. Val	atg M <b>et</b>	gct	gag Glu	aga Arg 160	557
tac T <u>yr</u>	aag Lys	atg Met	ctg Leu	atc Ile 165	Pro	ttt Phe	agc Ser	aac Asn	Pro 170	Arg	g gtg g Val	ctt Leu	cco Pro	ggg Gly 175	g ccc 7 Pro 5	605
ttc Phe	tca Ser	tac Tyr	acg Thr 180	Val	gtg Val	ctg Leu	tat Tyr	ggt Gly 185	. bro	gca Ala	a ggc a Gly	: ctt Leu	ggg Gly 190	y Lys	a acc 5 Thr	653
acg Thr	ctg Leu	gcc Ala 195	Gln	aaa Lys	cta Leu	atg Met	cta Leu 200	. Asp	tgg Trp	g gca Ala	a gag a Glu	gad Asp 205	) Ası	c cto n Lei	atc lle	701

FIG. 1A

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cac His	aaa Lys 210	ttc Phe	aaa Lys	tat Tyr	gcg Ala	ttc Phe 215	tac Tyr	ctc Leu	agc Ser	cāc Cāc	agg Arg 2 <b>20</b>	gag Glu	ctc Leu	agc ( Ser /	cgc Arg	749
ctg Leu 225	ggc Gly	ccg Pro	tgc Cys	agt Se <b>r</b>	Phe 230	gca Ala	gag Glu	ctg Leu	gtc Val	ttc Phe 235	agg Arg	gac A <b>sp</b>	tgg Trp	Pro	gaa Glu 240	79 <b>7</b>
ttg Leu	cag Gln	gat Asp	gac Asp	att Ile 245	cca Pro	cac	atc Ile	cta Leu	gcc Ala 250	caa Gln	gca Ala	Arg Cāg	aaa Lys	atc Ile 255	ttg Leu	845
ttc Phe	gtg Val	att Ile	gac Asp 260	ggc Gly	ttt Phe	jat Asp	gag Glu	ctg Leu 265	gga Gly	gcc Ala	gca Ala	cct Pro	ggg Gly 270	gcg Ala	ctg Leu	893
atc Ile	gag Glu	gac Asp 275	atc -Ile	tgc Cys	gg <b>g</b>	gac Asp	tgg Trp 280	gag Glu	aag Lys	aag Lys	aag Lys	ccg Pro 285	gtg Val	ccc Pro	gtc Val	941
ctc Leu	ctg Leu 290	ggg Gly	agt Ser	ttg Leu	ctg Leu	aac Asn 295	agg Arg	gtg Val	atg Met	tta Leu	ccc Pro 300	aag Lys	gcc Ala	gcc Ala	ctg Leu	9 <b>89</b>
ctg Leu 305	gtc Val	acc Thr	acg Thr	cgg Arg	ccc Pro 310	agg Arg	gcc Ala	ctg Leu	agg Arg	gac Asp 315	ctc Leu	cgg Arg	atc Ile	ctg Leu	gcg Ala 320	1037
g <b>ag</b> Glu	gag Glu	ccg Pro	atc Ile	tac Tyr 325	ata Ile	agg Arg	gtg Val	gag Glu	ggc Gly 330	ttc Phe	ctg Leu	gag Glu	gag Glu	gac Asp 335	aag Lys	1085
agg Arg	gcc Ala	tat Tyr	ttc Phe 340	Leu	aga Arg	cac His	ttt Phe	gga Gly 345	gac Asp	gag Glu	gac Asp	caa Gln	gcc Ala 350	Met	cgt Arg	1133
gc <b>c</b> Ala	ttt Phe	gag Glu 355	Leu	atg Met	agg Arg	agc Ser	aac Asn 360	Ala	gcc Ala	ctg Leu	tto Phe	cag Gln 3 <b>65</b>	ctg Leu	gg <b>c</b>	tcg Ser	1181
gcc Ala	2 ccc 2 Pro 370	Ala	gtg Val	tgc Cys	tgg Trp	atc Ile 375	Val	tgc .Cys	acg Thr	act Thr	ctg Leu 380	ı Lys	, ctg Leu	r cag i Gln	atg Met	1229
gaq Glu 385	Lys	ggg Gly	gag Glu	gac Asp	ccg Pro 390	Val	ccc. Pro	acc Thr	tgo Cys	cto Lev 395	ı Thi	cgo Aro	acq Thr	g ggg	Leu 400	1277
tto Phe	: ctg	cgt Arg	tto Phe	cto Leu 405	ı Cys	agc Ser	: cgg	g tto g Phe	2 CCC 2 Pro 410	Glr	g ggo	gca Ala	a caq a Glr	g cto n Leu 415	g cgg i Arg	1325
gg¢ Gly	gcg Ala	cto Lev	g cgg 1 Arg 420	, Thr	g ctg : Leu	ago Ser	cto Lev	2 ctq 1 Lev 425	ı Ala	e geo a Ala	g cad a Glr	g ggo n Gly	c cto y Lei 430	ı Trp	g gcg Ala	1373

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												ctc Leu 445				1421
												ctc Leu				1469
												agc Ser				15 <b>17</b>
												gag Glu				1565
												aag Lys				1613
												gca Ala 525				16 <b>61</b>
												ttg Leu				1709
												ttg Leu				1757
												gac Asp				1805
												ctg Leu		Lys		1853
gtg Val	atg Met	gct Ala 595	cag Gln	ttc Phe	aaa Lys	g <b>aa</b> Glu	ata Ile 600	tcc Ser	ctg Leu	cac	tta Leu	aat Asn 605	Ala	gta Val	gac Asp	1901
												aac Asn				1949
						Lys					Glu				gcg Ala 640	1997
ict Ser	gaa	tca	gac	gcc Ala	gag	gtt	gag	aga Ara	tcc	cag	gat	gat Asr	cac	r cac	atg	2045

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											gga Gly					2 <b>093</b>
ctg L <b>eu</b>	atg M <b>et</b>	ggt Gly 675	cta Leu	gca Ala	atc	aat Asn	gat Asp 680	agc Ser	ttt Phe	ctc	agt Ser	gcc Ala 685	toc Ser	cta Leu	gta Val	2141
agg Arg	atc Ile 690	ctg Leu	tgt Cys	gaa Glu	caa Gln	ata Ile 695	gcc Ala	tct Ser	gac Asp	acc Thr	tgt Cys 700	cat His	ctc Leu	cag Gln	aga Arg	2189
											cat His					2 <b>237</b>
cta Leu	gct Ala	ctt Leu	cga Arg	ggt Gly 725	cac His	aag Lys	act Thr	gta Val	acg Thr 730	tat Tyr	ctg Leu	acc Thr	ctt Leu	caa Gln 735	ggc Gly	2285
											g <b>ag</b> Glu					2333
											tct Ser					2381
											gaa Glu 780					2 <b>429</b>
ctg Leu 785	acg Thr	tg <b>c</b> Cys	gta Val	aac Asn	ctc Leu 790	tcc Ser	gac Asp	aat Asn	gag Glu	ctt Leu 795	ctg Leu	gat Asp	gag Glu	ggt Gly	gct Ala 800	2 <b>477</b>
											tgc Cys					2 <b>525</b>
ttg Leu	tcg Ser	ttg Leu	gaa Glu 820	aac Asn	tgt Cys	cac His	ctt Leu	aca Thr 825	gaa Glu	gcc Ala	aat Asn	tgc Cys	aag Lys 830	gac Asp	ctt Leu	2 <b>573</b>
											cac His					2621
											ctg Leu 860					2 <b>669</b>
											ctt Leu					2717

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ata act Ile Thr	agc gat Ser Asp	ggc to Gly Cy 885	dc tdc dc Cha	gat Asp	ctc Leu	aca Thr 890	aag Lys	ctt Leu	ctc Leu	caa Gln	gaa Glu 895	aaa Lys	2765
tca agc Ser Ser	ctg ttg Leu Leu 900	Cys L	tg gat eu Asp	ctg Leu	999 905	ctg Leu	aat Asn	cac His	ata Ile	gga Gly 910	gtt Val	aag Lys	2813
gga atg Gly Met	aag ttc Lys Phe 915	ctg to	gt ga <b>g</b> ys Glu	gct Ala 920	ttg Leu	agg Arg	aaa Lys	cca Pro	ctg Leu 925	t gc Cys	aac Asn	ttg Leu	2861
aga tgt Arg Cys 930	ctg tgg Leu Trp	ttg t Leu T	gg gga rp Gly 935	tgt Cys	tcc Ser	atc Ile	cct Pro	ccg Pro 940	ttc Phe	agt Ser	tgt Cys	gaa Glu	29 <b>09</b>
gac ctc Asp Leu 945	tgc tct Cys Ser	Ala L	tc agc eu Ser 50	aac Asn	cag Gln	agc Ser	ctc Leu 955	gtc Val	act Thr	ctg Leu	gac Asp	ctg Leu 960	2957
ggt cag Gly Gln	aat ccc Asn Pro	ttg g Leu G 965	gg tot ly Ser	agt Ser	gga Gly	gtg Val 970	aag Lys	atg Met	ctg Leu	ttt Phe	gaa Glu 975	acc Thr	3005
ttg aca Leu Thr	tgt tcc Cys Ser 980	: Ser G	gc acc	ctc Leu	cgg Arg 985	aca Thr	ctc Leu	agg Arg	ttg Leu	aaa Lys 9 <b>90</b>	Ile	gat Asp	3053
gac ttt Asp Phe	aat gat Asn Asp 995	gaa c Glu L	tc aat eu Asn	aag Lys 100	Leu	ctg Leu	gaa Glu	gaa Glu	ata Ile 100	Glu	. gaa . Glu	aaa Lys	3101
aac cca Asn Pro 101	caa cto Gln Leo O	g att a 1 Ile I	tt gat le Asp 101	Thr	gag Glu	aaa Lys	cat His	cat His 102	Pro	tgg Trp	g gca Ala	gaa Glu	3149
agg cct Arg Pro 1025	tct tct Ser Sei	c His A	sac tto Asp Phe 1030	atg Met	atc Ile								3176
TGCCTGT GCTAGAT TTACATA	CCC CGAG GAC TCC GTT TTAG TGA AAT	ICTCCTO SCCATGI ATCTGTI	C CCCGG	GCCCC GCCTC	T AC	CCCI TTTP	CAGO TACO	GAT TGC	CACAC	SAGT	TCAT	TTGCTGG ATCTTTG	3 <b>296</b> 3 <b>356</b>

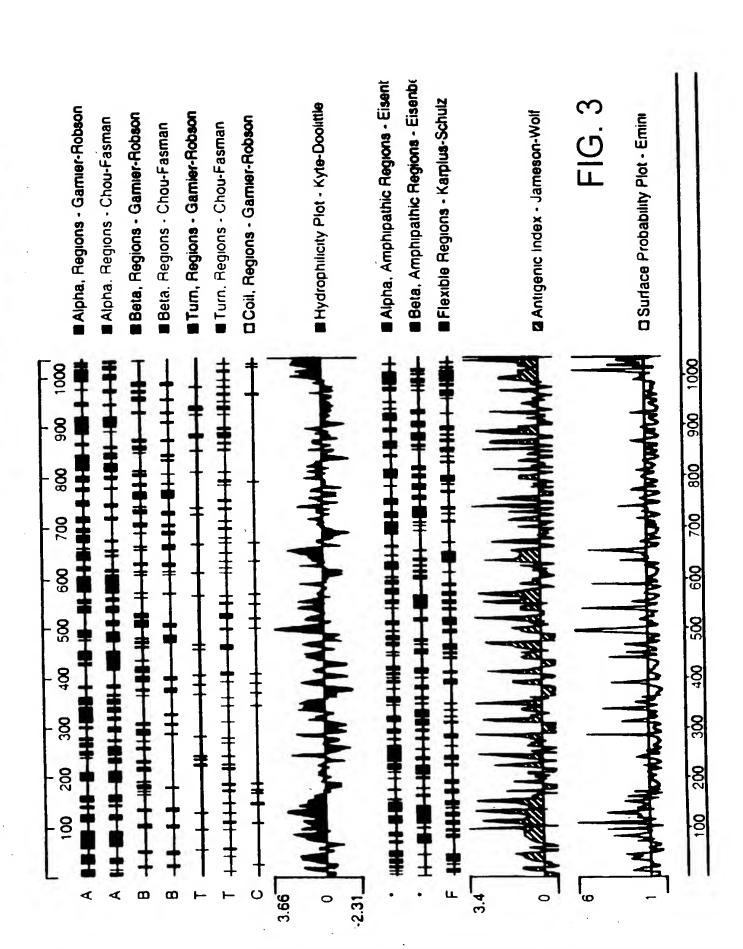
FIG. 1E

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cact	cctg	ga t	cgag	ccaa aag	c ag atg	gaga. gca	actt agc	tct acc	gtgt cgc	gga tgc	ccga aag		ta ad gcc a	ggaco agg 1	ggaca cetga tac Tyr	60 120 171
ctg Leu	gag Glu	gac Asp	ctg Leu 15	gag Glu	gat Asp	gtg Val	gac Asp	ttg Leu 20	aag Lys	aaa Lys	ttt Phe	aag ( Lys	atg Met 25	cac His	tta Leu	219
gag Glu	gac Asp	tat Tyr 30	cct Pro	ccc Pro	cag Gln	aag Lys	ggc Gly 35	tgc Cys	atc Ile	ccc Pro	ctc Leu	ccg Pro 40	agg Arg	ggt Gly	cag Gln	267
aca Thr	gag Glu 45	aag Lys	gca Ala	gac Asp	cat His	gtg Val 50	gat Asp	cta Leu	gcc Ala	acg Thr	cta Leu 55	atg Met	atc Ile	gac Asp	ttc Phe	315
aat Asn 60	Gly ggg	gag Glu	gag Glu	aag Lys	gcg Ala 65	tgg Trp	gcc Ala	atg Met	gcc Ala	gtg Val 70	tgg Trp	atc Ile	ttc Phe	gct Ala	gcg Ala 75	363
atc Ile	aac Asn	agg Arg	aga Arg	gac Asp 80	ctt Leu	tat Tyr	gag Glu	aaa Lys	gca Ala 85	aaa Lys	aga Arg	gat Asp	gag Glu	ccg Pro 90	aag Lys	411
tgg Trp	ggt Gly	tca Ser	gat Asp 95	aat Asn	gca Ala	cgt Arg	gtt Val	tcg Ser 100	aat Asn	ccc Pro	act Thr	gtg Val	ata Ile 105	tgc Cys	cag Gln	459
gaa Glu	Asp	Ser	Ile	Glu	Glu	Glu	Trp	Met	Gly	Leu	Leu	gag Glu 120	Tyr	ctt Leu	tcg Ser	507
aga Arg	atc Ile 125	tct Ser	att Ile	tgt Cys	aaa Lys	atg Met 130	aag Lys	aaa Lys	gat Asp	tac Tyr	cgt Arg 135	aag Lys	aag Lys	tac Tyr	aga Arg	555
aag Lys 140	tac Tyr	gtg Val	aga Arg	agc Ser	aga Arg 145	ttc Phe	cag Gln	tgc Cys	att Ile	gaa Glu 150	Asp	agg Arg	aat Asn	gcc Ala	cgt Arg 155	603
ctg Leu	ggt Gly	gag Glu	agt Ser	gtg Val 160	Ser	ctc Leu	aac Asn	aaa Lys	cgc Arg 165	Tyr	aca Thr	cga Arg	ctg Leu	cgt Arg 170	Leu	651
atc Ile	aag Lys	gag Glu	cac His 175	Arg	agc Ser	cag Gln	cag Gln	gag Glu 180	. Arg	gag Glu	cag Gln	gag Glu	ctt Leu 185	Leu	gcc Ala	699
atc Ile	Gly	aag Lys 190	Thr	aag Lys	acg Thr	tgt Cys	gag Glu 195	Ser	ccc Pro	gtg Val	agt Ser	ccc Pro 200	Il∈	aag Lys	atg Met	747
gag Glu	ttg Leu 205	Let	ttt Phe	gac Asp	ccc Pro	gat Asp 210	Asp	gag Glu	cat His	tct Ser	gaç Glu 215	ı Pro	gto Val	g cac His	acc Thr	795

FIG. 4A

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		gtg Val		_			_							_	_		843	
	_	atg Met	_	_			_	_						_			891	
	_	tat Tyr	_					-		-		-				_	939	
		agc Ser	_														987	
		atc Ile 285		_			_				-					_	1035	
	_	ggc Gly		-		-			_		-					-	1083	}
		tgc Cys		_		_	_	_				-			_	_	1131	-
	_	ctc Leu		_	•	-	-				-		_				1179	ð
		aga Arg															1227	7
		cat His 365	_	_							_				_		1275	5
		ttc Phe														agt Ser 395	1323	3
	_		_	_			_				-	-				ctg Leu	137	1
•															Ser	ggc Gly	141	9
														Tyr		ttc Phe	146	7

FIG. 4B

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	ctt Leu 445		_		-						_	_				1515
	tgc Cys	_						_		_	_	-	-			1563
	aac Asn	-			_					-						1611
_	cag Gln	_			-		-		_		_		_			1659
-	gaa Glu		_	_		_			_				_			1707
_	gag Glu 525			-	-	_			_	•	-		-	_	-	1755
	agg Arg	-		_			_	_	-	_			_	_	_	1803
	aca Thr	-									_	-				1851
	ttt Phe	_	_	_						-		-	-			1899
	tac	tta														
261	Tyr	-	-	_			_	_	_			_	caa			1947
ctg	Tyr gag Glu 605	Leu 590 ctg	Glu	Lys	Lys tgg	Leu	Ser 595 gaa	Cys	Lys	Ile gcc	Ser	Gln 600 gct	caa Gln aaa	Ile aag	Arg	1947 1995
ctg Leu cag	gag Glu 605 atc	Leu 590 ctg Leu	Glu ctg Leu ccc	Lys aaa Lys agc	Lys tgg Trp	att Ile 610	Ser 595 gaa Glu gaa	Cys gtg Val ttg	Lys aaa Lys ttc	Ile gcc Ala tac	Ser aaa Lys 615	Gln 600 gct Ala ttg	caa Gln aaa Lys	Ile aag Lys gag	Arg ctg Leu	
ctg Leu cag Gln 620 cag	gag Glu 605 atc	Leu 590 ctg Leu cag Gln	Ctg Leu CCC Pro	Lys aaa Lys agc Ser	tgg Trp cag Gln 625	att Ile 610 ctg Leu	Ser 595 gaa Glu gaa Glu	Cys gtg Val ttg Leu gcc	Lys  aaa Lys  ttc Phe	gcc Ala tac Tyr 630	aaa Lys 615 tgt Cys	Gln 600 gct Ala ttg Leu	caa Gln aaa Lys tac Tyr	Ile aag Lys gag Glu	Arg  ctg Leu  atg Met 635  att Ile	1995

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att Ile	gag Glu	aac Asn 670	tgt Cys	cat His	cgg Arg	gtg Val	gag Glu 675	tca Ser	ctg Leu	tcc Ser	ctg Leu	ggg Gly 680	ttt Phe	ctc Leu	cat His	2187
aac Asn	atg Met 685	ccc Pro	aag Lys	gag Glu	gaa Glu	gag Glu 690	gag Glu	gag Glu	gaa Glu	aag Lys	gaa Glu 695	ggc Gly	cga Arg	cac His	ctt Leu	2235
gat Asp 700	atg Met	gtg Val	cag Gln	tgt Cys	gtc Val 705	ctc Leu	cca Pro	agc Ser	tcc Ser	tct Ser 710	cat His	gct Ala	gcc Ala	tgt Cys	tct Ser 715	2283
cat His	gga Gly	ttg Leu	gtg Val	aac Asn 720	agc Ser	cac His	ctc Leu	act Thr	tcc Ser 725	agt Ser	ttt Phe	tgc Cys	cgg Arg	ggc Gly 730	ctc Leu	2331
ttt Phe	tca Ser	gtt Val	ctg Leu 735	agc Ser	acc Thr	agc Ser	cag Gln	agt Ser 740	cta Leu	act Thr	ga <b>a</b> Glu	ttg Leu	gac Asp 745	ctc Leu	agt Ser	2379
gac Asp	aat Asn	tct Ser 750	Leu	Gly	gac Asp	cca Pro	999 Gly 755	atg Met	aga Arg	gtg Val	ttg Leu	tgt Cys 760	gaa Glu	acg Thr	ctc Leu	2427
cag Gln	cat His 765	Pro	ggc Gly	tgt Cys	aac Asn	att Ile 770	cgg Arg	aga Arg	ttg Leu	tgg Trp	ttg Leu 775	Gly	cgc Arg	tgt Cys	ggc Gly	2475
ctc Leu 780	Ser	cat His	gag Glu	tgc Cys	tgc Cys 785	ttc Phe	gac Asp	atc Ile	tcc Ser	ttg Leu 790	Val	ctc Leu	agc Ser	ago Ser	aac Asn 795	2523
cag Gln	aag Lys	ctg Leu	gtg Val	gag Glu 800	Leu	gac Asp	ctg Leu	agt Ser	gac Asp 805	Asn	gcc	ctc Leu	ggt Gly	gac Asp 810	ttc Phe	2571
gga Gly	ato Ile	: aga : Arç	ctt Leu 815	Leu	tgt Cys	gtg Val	gga Gly	ctg Leu 820	Lys	cac His	cto Lei	g ttg ı Lev	tgo Cys 825	: Ası	ctg n Leu	2619
aag Lys	aag Lys	cto Lev 830	ı Trp	ttg Lev	gtc Val	agc Ser	tgo Cys 835	Cys	cto Leu	aca Thr	tca Sea	a gca r Ala 840	a Cys	tg: S Cy:	cag s Gln	2667
gat Asp	ctt Lei 845	ı Ala	a tca a Ser	gta Val	ı ttg Leu	ago Ser 850	Thi	ago Ser	cat His	tco Sei	c cto Lev 85	u Thi	e aga	a cto g Le	c tat u Tyr	2715
gto Val 860	Gl	g gaq y Glu	g aat ı Asr	gco Ala	ttg Lev 865	ı Gly	ı gad 7 Ası	c tca p Ser	a gga Gl:	a gto y Val 870	l Al	a at a Il	t tt e Le	a tg u Cy	t gaa s Glu 875	2763
aaa Lys	a gco s Ala	c aad a Ly:	g aat s Asr	cca Pro 880	o Glr	g tgt n Cys	aa Ası	c cto n Lei	g cad 1 Gli 88	n Ly	a ct s Le	g gg u Gl	g tt y Le	g gt u Va 89	g aat 1 Asn 0	2811

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tct ggc ctt Ser Gly Leu				Ala							2859
act aat cag Thr Asn Gln 910	Asn Leu										2907
gac aag ggg Asp Lys Gly 925											2955
aag ctt cag Lys Leu Gln 940		-	_								3003
tgc tgg gat Cys Trp Asp		Thr Leu									3051
ctg agc ctg Leu Ser Leu				y Asp							3099
tgt gaa gtg Cys Glu Val 99	. Leu Lys							Leu			3147
tct gaa atg Ser Glu Met 1005			Glu Th		_	-	Leu				3195
caa gaa gaa Gln Glu Glu 1020						Glu					3243
gagtggaaac ggtggagaga gtgtcggaga acgccagggt gcctcagtta ctttctttat ttctgtttac cagaactagt tttttgtaat attcaggaat aaaaaaaaaa	gctgcgat agagagct gaggaaga gaggatgt ttttctct ttttgctc tgactata agttttgt atgtaaaa	cc atcca tg ccgac ca ccagg tc ctctt tc tctgt at atcat tt tctaa	ggcca a gatgc c acaat g ggtga c ctaac t cattc c ttgaa a taaga a	gacca ttcct acagc ctcat ttctt cgcta tttta aaatc	cagc gtgc atcg gtaa tttc actt tggc	tctc agac ggtc ttac ctac tctc agc	gtga gctt gttg gctc tctt atta tttg	tcc ggg ttc att ttt act tat	ttect catc tcat caat ttet gacc ttat ctgg	eggtgga etccttt ecacagc aaagca etctttg eataaca ettaaat gttgaaa	3303 3363 3423 3483 3543 3603 3663 3723 3783 3843 3857

FIG. 4E

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NOVEL MOLECULES OF THE PYRIN DOMAIN PROTEIN

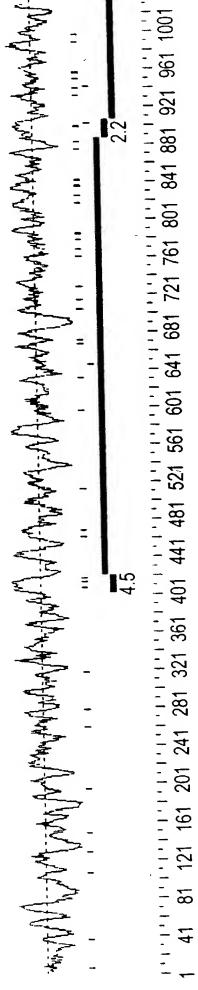
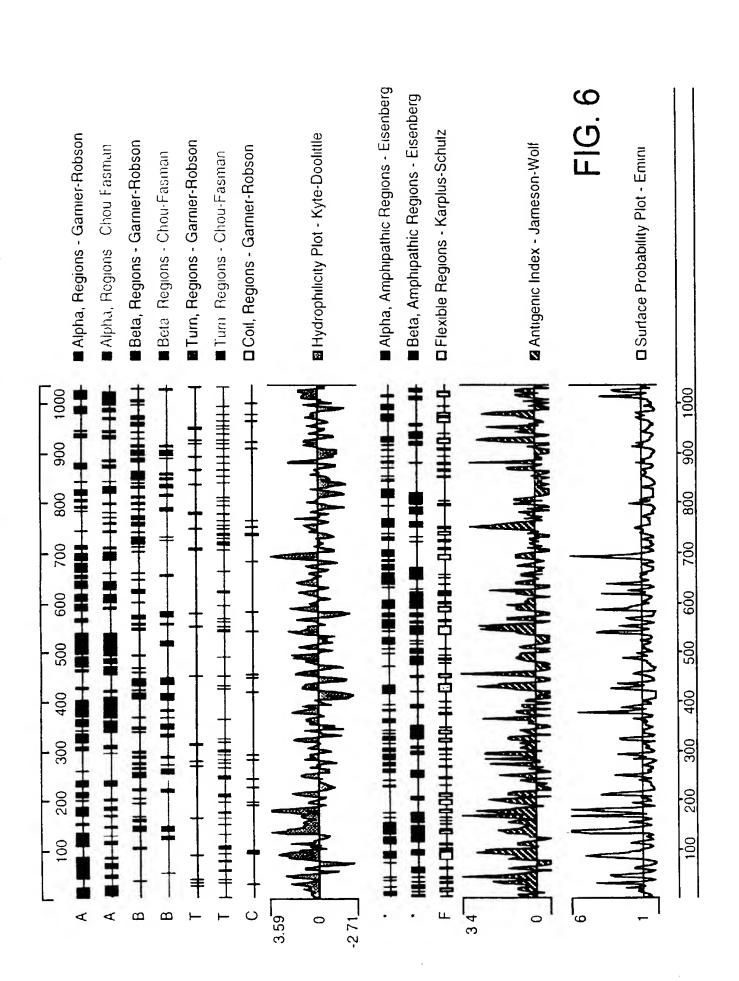


FIG. 5

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NOVEL MOLECULES OF THE PYRIN DOMAIN PROTEIN
FAMILY AND USES THEREOF



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NOVEL MOLECULES OF THE PYRIN DOMAIN PROTEIN FAMILY AND USES THEREOF

Majority	NES1-PYRIN DOMAIN PYRIN-PYRIN DOMIAN CARD5-PYRIN DOMAIN CARD7-PYRIN DOMAIN	Majority	NES1-PYRIN DOMAIN PYRIN-PYRIN DOMIAN CARD5-PYRIN Domain CARD7-PYRIN DOMAIN
DXLLXXLEXLXXEELKKFKLLLXNXSXXXEXSRIPRXQXX Majority 10 20 30 40	1 FNLOAL LFQLSQDFLSFFFFFFFFPAH LQKFHKEVD 1 DHLLST FEVPYDFEFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFF	KADGXXLAXXLVTXYGEXYAVELA LQVLEXMGLRXLA 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	41 RAPCKOLVEILTTHC-DSTWYFMASLATKHKHRMDHS 41 SMDALDLTDKLYTTHGAFTGAFTT-ANTRDHGE

FIG. 7

f 30

838

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FIG. 8A

752

a[+8+[++

u

from 726 to 752: score 0.1

œ

of

LER\_RI\_2: domain l

-->npstretdtsnNklgdeGarataeatks<

L L++N+ d+

HKTVTYLTLQGND-QDDMFPALCEVLRH

726

NBS1

Ш of .8, from 782 to 809: score 20.8 \*->npstretdtsnNklgdeGarataeatks< ~ LER\_RI\_2: domain

309 n+sL +Ls+N l deGa+ L NOSLICVNLSDNELLDEGAKL

FIG. 8B

782

NBS1

W score 21 -->npstretdtanNklgdeGarataeatks from 811 to 838: 8 of LER\_RI\_2: domain

KCFLQRLSLENCHLTEANCKDLAAVLVV \*\* L\*\*L\*L\*n\*\*1\*\*\* \*\* La\*\*L

811

NBS1

FIG. 8C

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0.56 11 998 山 ->npstretdtsnNklgdeGarataeatks Srelthlclaknpigntgvkflceglry G++ L+8+L+ SCOL 866: to L+ N++g 839 from æ of 839 domain NBS1

895 ECKLQTLVLWNCDITSDGCCDLTKLLQE ->npstretdtsnNklgdeGaraLaeatks from 868 to 895: score ++[++[ [+n++++ +G+ of LRR\_RI\_2: domain

868

NBS1

Ħ 923 山 score 22 ->npstretdtsnNklgdeGaraLaeatks< KSSLLCLDLGLNHIGVKGMKFLCEALRK ++8F+ LdL+ N++g +G++ L+eaL+ 896 to 923: from œ of 9 896 domain NBS1 LRR\_RI\_2:

lcozras .azzcínt

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NOVEL MOLECULES OF THE PYRIN DOMAIN PROTEIN FAMILY AND USES THEREOF

0.26 Ħ Ш from 925 to 952: score 15 -->npstretdtsnNklgdeGaraLaeaLks< + [++a[+ +++Lr L+L+++ + + 8 of LRR\_RI\_2: domain

LCNLRCLWLWGCSIPPFSCEDLCSALSN FIG. 8G

928

NBS1

952

979 回 8, from 953 to 979: score 14.0 -->npstretdtsnNklgdeGarataeatks< -QSLVTLDLGQNPLGSSGVKMLFETLTC +3F +LdL++N+1g +G++ L B+L+ of œ 953 LER\_RI\_2: domain NBS1

FIG. 8H

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FAMILY AND USES THEREOF

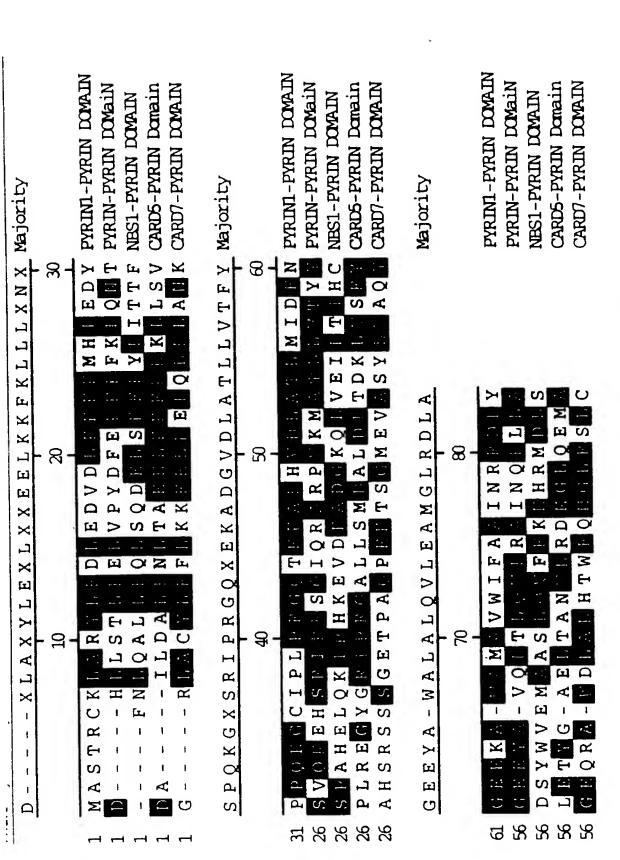


FIG. 9A

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NOVEL MOLECULES OF THE PYRIN DOMAIN PROTEIN FAMILY AND USES THEREOF

90 90 98 89 89

**43** ANKAHS **PYPAF1** pyrin CARD7 NBSI POPI ASC

RMLEE ONI IN R × GEE **PYPAF1** CARD7 pyrin NBSI POPI ASC

Decoration 'Decoration #1': Shade (with solid black) residues that match the Consensus exactly.

Decoration 'Decoration #2': Shade (with solid black) residues that match the Consensus exactly.

Decoration 'Decoration #3': Box residues that match the Consensus exactly.

FIG. 9B



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NOVEL MOLECULES OF THE PYRIN DOMAIN PROTEIN

```
LRR: domain 1 of 9, from 740 to 767: score 10.9, E = 25
                                                        FIG. 10A
                   *->nLeeLdLsnN.Lt...slppglfsnLp<-*
                      +L+eLdLs+N+L +++ + +++++
    pyrin-1
              740
                     SLTELDLSDNsLGdpgmRVLCETLQHPG
                                                     767
LRR: domain 2 of 9, from 769 to 796: score 2.3, E = 4.6e+02
                   *->nLeeLdLsnN.Lt....slppglfsnLp<-*
                                                          FIG. 10B
                     n+++L+L +++L+++ ++++ ++s+ +
    pyrin-1
                     NIRRLWLGRCgLSheccfDISL-VLSSNQ
              769
                                                      796
LRR: domain 3 of 9, from 797 to 821: score 9.7, E = 39
                                                       FIG. 10C
                   *->nLeeLdLsnN.Lt..slppglfsnLp<-*
                      +L eLdLs+N L + ++ l+ +L+
              797
    pyrin-1
                     KLVELDLSDNaLGdfGIRL-LCVGLK
                                                   821
LRR: domain 4 of 9, from 826 to 849: score 4.1, E = 2.5e+02
                   *->nLeeLdLsnN.LtslppglfsnLp<-*
                                                      FIG. 10D
                     nL++L+L ++ Lts
    pyrin-1
                     NLKKLWLVSCcLTSACCQDLASVL
              826
                                                 849
LRR: domain 5 of 9, from 854 to 878: score 0.6, E = 8.2e+02
                   *->nLeeLdLsnN.Lt..slppglfsnLp<-*
                                                        FIG. 10E
                     +L++L++ N L ++++ 1+++
     pyrin-1
              854
                     SLTRLYVGENaLGdsGVAI-LCEKAK
                                                   878
LRR: domain 6 of 9, from 883 to 906: score 5.1, E = 1.8e+02
                   *->nLeeLdLsnN.LtslppglfsnLp<-*
                     nL++L L n +Lts+ +++s+
                                                       FIG. 10F
    pyrin-1
              883
                     NLQKLGLVNSgLTSVCCSALSSVL
                                                 906
LRR: domain 7 of 9, from 911 to 935: score 10.2, E = 32
                   *->nLeeLdLsnN.Lt..slppglfsnLp<-*
                                                        FIG. 10G
                     nL++L+L++N+L+++++ l+++L
    pyrin-1
                     NLTHLYLRGNtLGdkGIKL-LCEGLL
              911
                                                   935
LRR: domain 8 of 9, from 940 to 967: score 5.8, E = 1.4e+02
                   *->nLeeLdLsnN.Lt....slppglfsnLp<-*
                                                          FIG. 10H
                      +L++L L+n++Lt++ +l+ l+ ++
     pyrin-1
              940
                     KLQVLELDNCnLTshccwDLST-LLTSSO
                                                      967
LRR: domain 9 of 9, from 968 to 991: score 8.4, E = 59
                   *->nLeeLdLsnN.LtslppglfsnLp<-*
                                                      FIG. 101
                      +L++L+L nN+L +1 f+
     pyrin-1
               968
                      SLRKLSLGNNdLGDLGVMMFCEVL
                                                 991
```

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NOVEL MOLECULES OF THE PYRIN DOMAIN PROTEIN

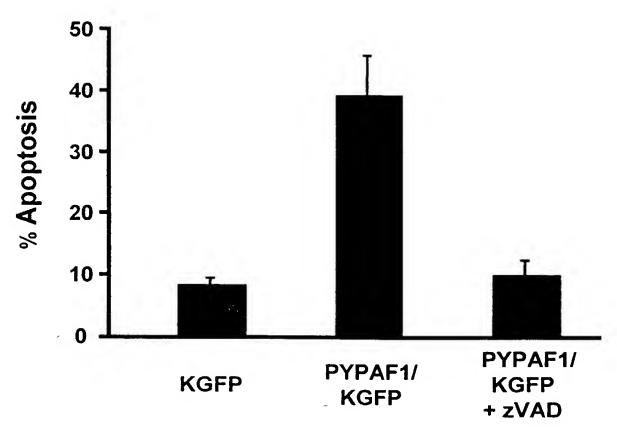
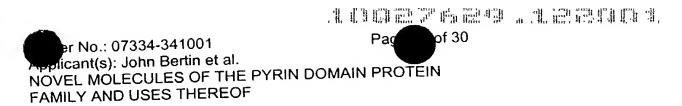
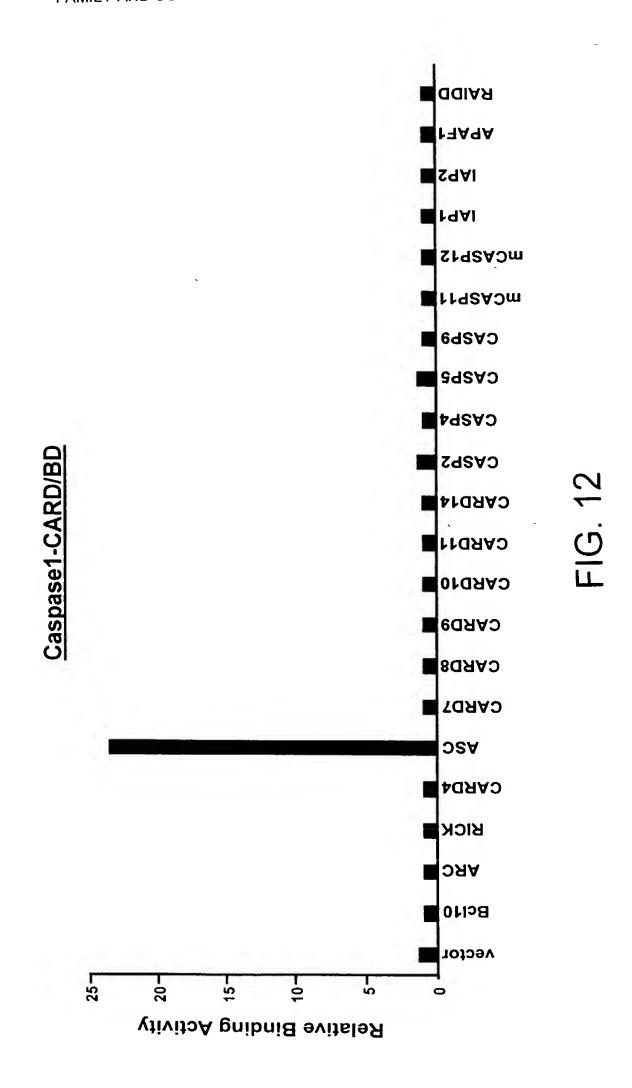


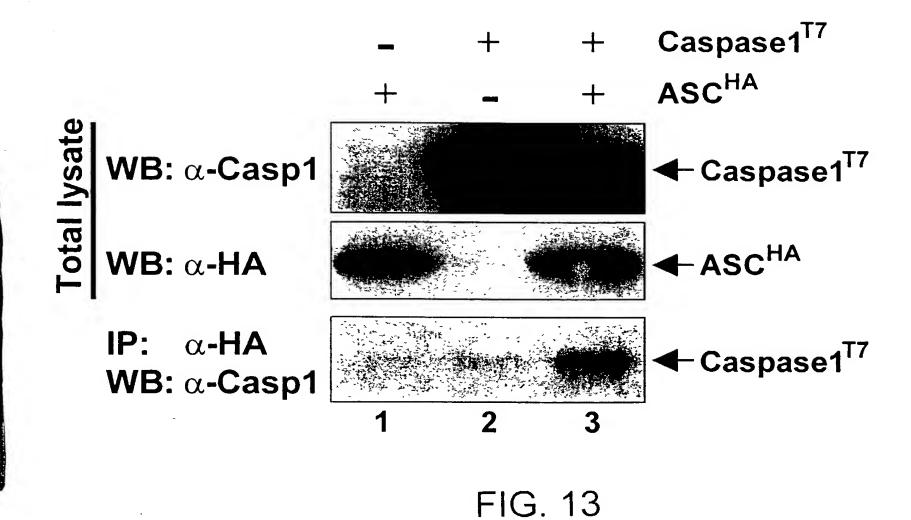
FIG. 11

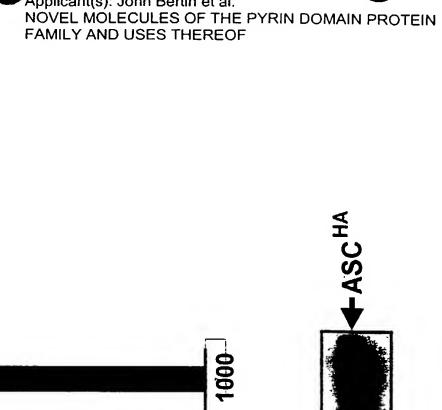




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NOVEL MOLECULES OF THE PYRIN DOMAIN PROTEIN





- 500

- 250

125

64

Relative MF- $\kappa B$  Activity

ASC DNA (ng)

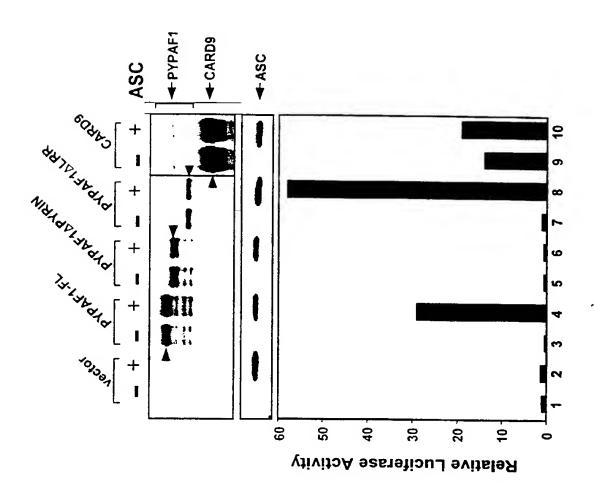
FIG. 14

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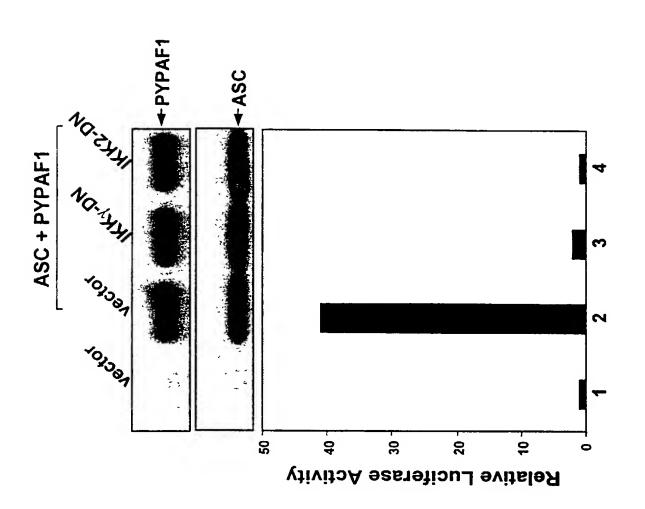
NOVEL MOLECULES OF THE PYRIN DOMAIN PROTEIN



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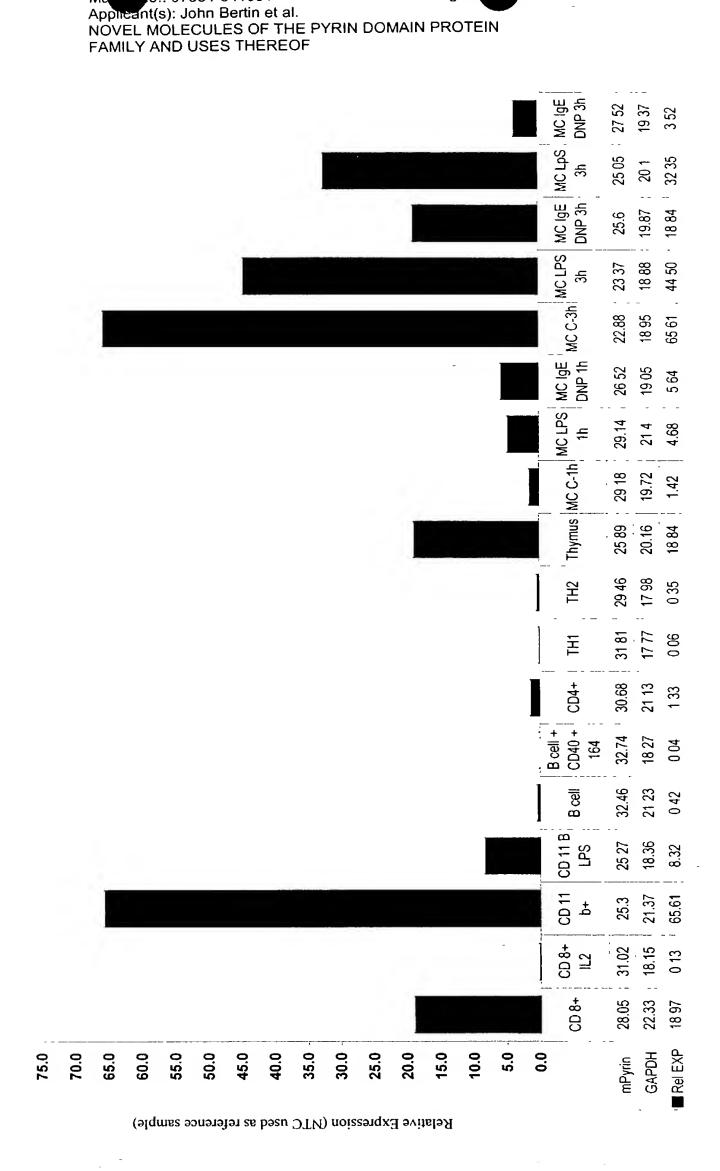
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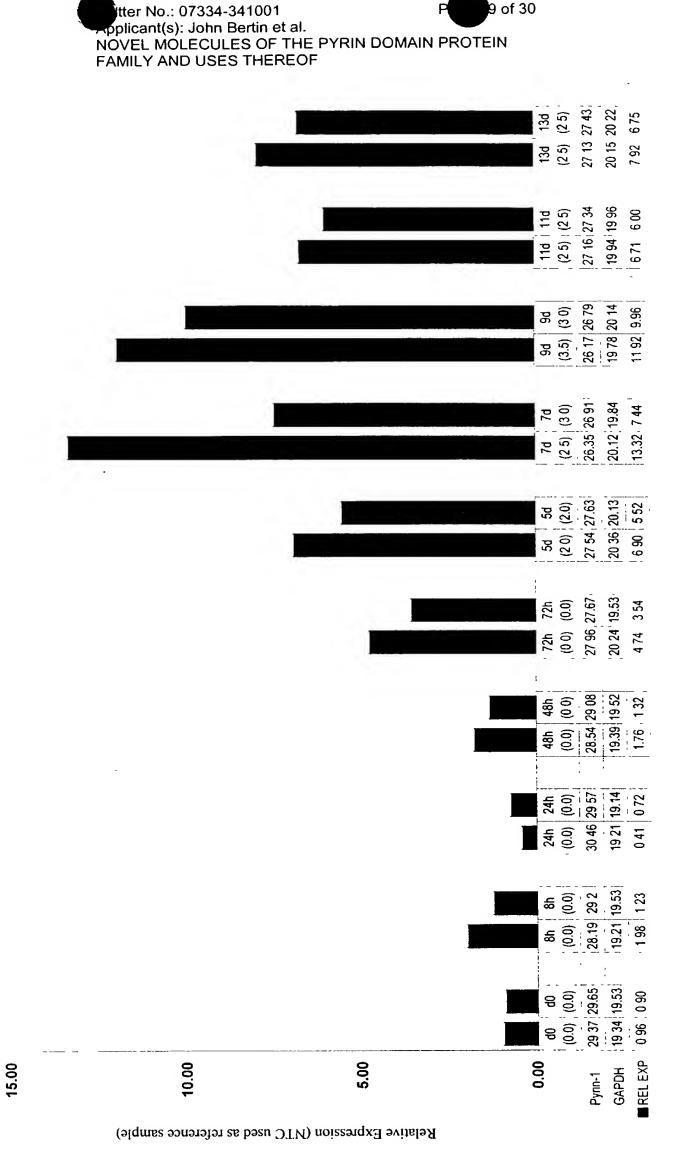
mPyrin Expression in Normal Mouse Cell Panel



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Pyrin-1 Expression in ABT Model



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Grade Grade Grade Grade 30.58 31.63: 29.3 29.28 6.48 | 3.17 | 4 71 | 20 05 23.31 23.33 ; 21.57 23 64 4-2 4-3 4-4 4-1 22.58 | 21.32 | 24.69 | 22.17 | 4.22 | 7.60 | 8.55 | 0.79 Grade Grade Grade Grade 30.47 | 28.36 | 31.56 | 32.48 34 3-1 3-2 3-3 Grade Grade Grade 32.36 32.63 31 67 2-2 2-3 21.42 21.44 22.7 Grade Grade Grade 29.5 32.08 32.55 31.05 20.07 22.64 21.66 21.35 1.45 | 1.44 | 0.53 | 1.20 <del>1.</del>3 7 33.62 31.61 34.68 33.93 21 74 20 03 23.67 22.96 Unt-1 Unt-2 Unt-3 Unt-4 0 33 | 0 48 | 0.50 0.27 Rel EXP GAPDH 15.0 10.0 5.0 0.0 Pyrin-1 20.0

Relative Expression (NTC used as reference sample)

Pyrin-1 Expression in CIA Model